I. THE SYNTHESIS OF COMPOUNDS RELATED TO INDOLE ALKALOIDS

II. THE ADDITION PRODUCTS OF ANILS AND ACID ANHYDRIDES

BY

JOHN CLARK LORENZ

B.S., Carnegie Institute of Technology, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1951

URBANA, ILLINOIS

1951

I. THE SYNTHESIS OF COMPOUNDS RELATED TO INDOLE ALKALOIDS

II. THE ADDITION PRODUCTS OF ANILS AND ACID ANHYDRIDES

BY

JOHN CLARK LORENZ

B.S., Carnegie Institute of Technology, 1948

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE COLLEGE OF THE
UNIVERSITY OF ILLINOIS, 1951

URBANA, ILLINOIS

1951

ACKNOWLEDGMENT

The author wishes to express his gratitude to Dr. H. R. Snyder for suggesting this study and for his invaluable advice and encouragement throughout its course. He is also indebted to the University of Illinois for Teaching Assistantships from 1948 to 1950 and for a University Fellowship during the academic year 1950-51

R. UNIV.
BIBLIOTHEEK
LEIDEN

I. THE SYNTHESIS OF COMPOUNDS RELATED TO INDOLE ALKALOIDS

Introduction

Recent studies of yohimbine and of certain of the curare alkaloids indicate that these substances contain the ring system of 1,2-(2,3-naphtho)-2-carboline. It has been shown that compounds having this nucleus can be synthesized from tryptamine and derivatives of homophthalic acid. The present investigation is an extension of previous work in this laboratory on the synthesis of 3-methoxyhomophthalic acid, and an attempt to use this compound in the synthesis of yohimbine or its isomers.

Discussion Of Results

3-Methoxyhomophthalic anhydride has been synthesized from 3-methoxybenzaldehyde by a modification of the method developed by Marshall (1) and from phenyl β-chloropropionate. The sequence of reactions for each synthetic route is discussed below.

3-Methoxybenzaldehyde was converted to 3-methoxycinnamic acid by heating it with malonic acid and a small amount of pyridine. The cinnamic acid was reduced to 3-methoxyhydrocinnamic acid by hydrogenation over Raney nickel at 30° and 100 atmospheres pressure. Low pressure reduction in acetic acid with Adams catalyst gave only mixtures. The hydrocinnamic acid was brominated to 3-methoxy-6-bromohydrocinnamic acid, cyclized to 4-bromo-7-methoxy-1-indanone, nitrosated to 2-isonitroso-4-bromo-7-methoxy-1-indanone, rearranged and hydrolysed to 3-methoxy-6-bromohomophthalic acid and debrominated to 3-methoxyhomophthalic acid by Marshall's methods. The rearrangement of 2-isonitroso-4-bromo-7-methoxy-1-indanone with *p*-toluenesulfonyl chloride gave reduced yields of 3-methoxyhomophthalic acid, and the isonitroso ketone was recovered unchanged when a rearrange-

ment with sulfuric acid at 0° was attempted.

Phenyl β-chloropropionate was rearranged and cyclized to 7-hydroxy-1-indanone by treatment with aluminum chloride and heat, and the indanone was methylated with dimethyl sulfate to give 7-methoxy-1-indanone. This compound was nitrosated with methyl nitrite in methanol and in ethyl acetate to give 2-isonitroso-7-methoxy-1-indanone, but the nitrosation in ethyl acetate produced only a small amount of the desired product. The indanone was rearranged with phosphorous pentachloride in ether and hydrolysed to 3-methoxyhomophthalic acid with aqueous potassium hydroxide.

3-Methoxyhomophthalic anhydride was prepared by heating the acid with acetyl chloride. An attempt to prepare the anhydride with acetic anhydride gave an unknown compound which probably had the formula $C_{19}H_{17}O_5$.

Condensation of 3-methoxyhomophthalic anhydride with tryptamine carried out in anhydrous benzene, toulene, pyridine or chloroform produced a substance which could not be obtained in crystalline form. When this substance was treated with phosphorous pentoxide it was recovered unchanged, and treatment with phosphorous oxychloride produced a tar from which no crystalline compounds could be isolated.

BIBLIOGRAPHY

1. C. D. Marshall, Thesis, Doctor of Philosophy, University of Illinois, 1949.

II. THE ADDITION PRODUCTS OF ANILS AND ACID ANHYDRIDES

Introduction

The recent observation that the addition product of acetic anhydride and benzalaniline reacts with ethyl alcohol to give a

compound in which an acetyl group has been replaced by an ethyl group led to the proposal of an entirely new structure for the addition product. It also suggested that such a reaction with the addition product might be general for all compounds containing the hydroxyl group and possibly the amino group. The present investigation was undertaken to determine the validity of the new structure, to examine the generality of the reaction of the addition product with alcohols and amines and to correlate the new findings with other reactions of anil-anhydride addition products.

Discussion Of Results

Additional evidence for the structure, N-(α-acetoxybenzyl)-acetanilide, of the addition product of benzalaniline and acetic anhydride has been found in its decomposition in alcoholic sodium ethoxide to benzaldehyde, acetanilide and ethyl acetate. The origin of cinnamic acid under such conditions is explained by the condensation of benzaldehyde and ethyl acetate to give ethyl cinnamate.

It has been shown that the addition of acetic anhydride to benzalaniline is catalyzed by acetic acid, trifluoroacetic acid and boron trifluoride.

The reaction of N-(α-acetoxybenzyl)acetanilide with ethanol to give N-(α-ethoxybenzyl)acetanilide (1,2) has been extended to include analgous reactions with *n*-propyl alcohol, isopropyl alcohol, *n*-butyl alcohol, benzyl alcohol, phenol, benzoic acid and piperidine. The reaction can be effected either with the reactants alone or in anhydrous hydrocarbon solvents. Indole, benzyl mercaptan, ethyl acetoacetate, benzonitrile, *p*-nitrobenzyl alcohol, glucose, N-methylaniline, dibutylamine and phthalimide failed to react with the addition product. Correlation of these observation in a general mechanism which involves initial hydrogen bonding of the hydroxyl or amino compound with the carbonyl oxygen of the acetyl groups of N-(α-acetoxybenzyl)acetanilide followed by a shift of electrons over a quasi-six-membered ring is proposed.

The possible application of the general mechanism to the reactions of benzalanthranilic acid and 2-benzalaminophenol with acetic, maleic and succinic anhydrides (3) is discussed.

BIBLIOGRAPHY

1. H. S. Angel and A. R. Day, J. Am. Chem. Soc., **72**, 3874 (1950).

2. H. R. Snyder, D. B. Bright and J. C. Lorenz, J. Am. Chem. Soc., **73**, 1836 (1951).

3. H. R. Snyder, R. H. Levine and P. F. Wiley, J. Am. Chem. Soc., **60**, 2025 (1938).

VITA

John Clark Lorenz was born on June 11, 1923 in Coshocton, Ohio. After graduating from Coshocton High School in 1941 he attended the Carnegie Institute of Technology for two years. In 1943 he entered the Army of the United States and served in the American and Southwest Pacific Theaters. Upon discharge from the Army in 1946 he returned to Carnegie Institute of Technology where he received the degree of Bachelor of Science in 1948. In September of that year he entered the Graduate College of the University of Illinois. He held Teaching Assistantships from September, 1948 to August, 1950 and a University Fellowship during the academic year 1950-51.

Digitized by the Internet Archive
in 2026

https://archive.org/details/IA41549816_0214